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10/070,084	03/07/2002	Clarence Webster Andrews III	PU3517USW	7283

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EXAMINER	
RAO, DEEPAK R	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 03/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,084	ANDREWS ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-7,9-14,18-20,23,25,26,28,29,34-36,40,43-51 and 54-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *2-3, 5, 9, 18-20, 23, 25, 34-36, 40, 45-47, 55, 58-62* is/are allowed.

6)☒ Claim(s) *4,6,10-12,14,28,29,43,48-51,54 and 57* is/are rejected.

7)☒ Claim(s) *7,13,26,44 and 56* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12222005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the amendment filed on December 22, 2005.

Claims 2-7, 9-14, 18-20, 23, 25-26, 28-29, 34-35, 40, 43-51 and 54-62 are pending in this application.

Election/Restrictions

Claim 12 (in part, drawn to compounds of formula (ID) wherein R^3 and R^4 together with the nitrogen atom to which they are attached form a heterocycle) is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on November 10, 2003. The above part of claim 12 falls within the invention of Group II (according to the modified restriction suggested by the applicant).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 28, 29, 48, 49, 50 and 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treatment of an HIV infection in a mammal by administering a compound in an amount effective to inhibit HIV reverse transcriptase, does not reasonably provide enablement for a method of treatment of HIV infection generally; or a method of inhibiting HIV reverse transcriptase generally. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The scope of the claims is not adequately enabled solely based on the activity related to HIV reverse transcriptase inhibitory activity provided in the specification. First, the instant claims cover a method of treatment of HIV infection generally, for which there is no enablement provided. The use disclosed in the specification is as pharmaceutical therapeutic agents having HIV reverse transcriptase inhibitory activity, useful to treat HIV infection. Test procedures and assays to measure HIV-1 reverse transcriptase (RT) inhibition activity are provided in the specification at pages 391-396 and IC_{50} values for some of the exemplified compounds are provided in Table 1. Based on this data, the instant claims recite 'a method of treatment of an HIV infection in a mammal' or 'a method of inhibiting HIV reverse transcriptase in a mammal'.

The instant claims 29, 50 and 51 are drawn to 'a method of inhibiting HIV reverse transcriptase in a mammal' wherein the claims do not specify whether or not the method is subjected to a mammal "in need of" of such inhibition. The instant claims appear to be 'reach

through' claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions, for which they lack written description and enabling disclosure in the specification thereby requiring undue experimentation for one of skill in the art to practice the invention.

Claims 28, 48 and 49 recite 'a method of treatment of an HIV infection in a mammal by administering the compound to said mammal'. There are several classes of anti-HIV medications that are known (see http://www.healthscout.com/template.asp?page=ency&ap=1&encyid=101#TreatmentofAIDSandHIVInfection):

1. Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs), such as Efavirenz (Sustiva), bind to and block the action of reverse transcriptase, a protein that HIV needs to reproduce.

2. Nucleoside Reverse Transcriptase Inhibitors (NRTIs), such as zidovudine (Retrovir), tenofovir DF (Viread), and stavudine (Zerit), are faulty versions of building blocks that HIV needs to make more copies of itself. When HIV uses an NRTI instead of a normal building block, reproduction of the virus is stalled.

3. Protease Inhibitors (PIs), such as lopinavir/ritonavir (Kaletra), disable protease, a protein that HIV needs reproduce itself.

4. Fusion Inhibitors, such as enfuvirtide (Fuzeon), are newer treatments that work by blocking HIV entry into cells.

As can be see from the above, anti-HIV medications include Protease inhibitors, Fusion inhibitors, etc. The instant compounds are disclosed to have HIV reverse transcriptase activity,

however, the claims recite a method of treatment of HIV infection generally. Therefore, one of ordinary skill would not know to extrapolate this test data to compounds generally in the treatment of HIV infection.

Applicant's arguments filed on December 22, 2005 have been fully considered. Applicant argued that 'applicants have shown activity against both HIV-1 and HIV-2 by a compound of the invention as HIV reverse transcriptase inhibitors'. Accordingly, it is suggested to amend claims 28, 48 and 49 to recite 'a method of treatment of an HIV infection in a mammal by administering a compound (of claim 2, claim 4 or claim 23) in an amount effective to inhibit HIV reverse transcriptase'.

2. Claims 6, 10, 12 and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds of formula (IA), (IC) or (ID) wherein X is O, does not reasonably provide enablement for compounds of formula (IA), (IC) or (ID) wherein X is C or N. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification fails to enable the preparation of the entire scope of the claimed compounds. The process schemes I-XXXIV (pages 35-72) in the specification provide the essential starting materials to prepare the claimed compounds wherein X is O, however, there is no disclosure of the sources of starting materials needed to prepare for compounds wherein X is C or N. The specification provides processes of preparing the compounds wherein the specific linking group X is O, however, does not provide any explanation or sources such that a person of

ordinary skill could prepare the entire scope of the instantly claimed compounds. The specification provides how to prepare some of the starting materials that are required for the preparation of compounds wherein X is O and provides Examples of products wherein X is O, however, the specification does not provide guidance as to how the other types of compounds wherein X is C or N are prepared, nor provides any Examples of such compounds. As can be seen from the structural formulae of the claims, X is a linking functional group that links the moiety $-CH(R^2)-CO-NR^3R^4$ to the phenyl ring and is recited to include the terms " C " and " N " and such linking groups generally comprise of $-CH_2-$, -CH(OH)-, -C(O)-, -NH-, $-N(CH_3)-$, etc.

In view of the lack of direction provided in the specification regarding starting materials, the lack of working examples and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention. The starting material sources necessary to obtain the instant compounds must have been available as of the filing date in order to provide an enabling disclosure. See *In re Howarth*, 654 F.2d 103, 210 USPQ 689 (CCPA 1981); *Ex parte Moersch*, 104 USPQ 122 (POBA 1954). Applicants should show that the sources of these starting materials was common knowledge or readily available at the time of filing.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 10, 29, 50 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. In claim 6, in the definition of R^4, the term "-$S(O)_2[COR^{11}]_n$ wherein n is 1, 2 or 3" is not understood. When n is 1, it is clear that the above term represents –$S(O)_2$-C(O)-R^{11}, however, when n is 2 or 3, it is not clear where the additional –$C(O)R^{11}$ groups are attached. The discrepancy is also found in claim 10.
2. Claim 6 recites the limitation ".... then R^1 cannot be C_{1-8} alkyl, C_{3-6} cycloalkyl, ..." in the proviso statement (a) (see page 6, line 4). There is insufficient antecedent basis for this limitation in the claim. The definition of R^1 in the claim does not include the terms C_{1-8} alkyl and C_{3-6} cycloalkyl.
3. In claim 29, it is recited that 'a method of inhibiting HIV reverse transcriptase comprising administering to a mammal', however, the claim does not specify that the compound is administered to 'a mammal **in need of**' the inhibiting activity. Claims 50 and 51 also contain the same discrepancy.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 4, 6, 10, 11, 14, 54 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wyatt et al. (J. Med. Chem. 1995). The reference teaches benzophenone compounds having HIV reverse transcriptase inhibitory activity, see the compounds in Table 1, particularly compound 1g. According to the instant claims, R^4 is a substituted aryl, e.g., a substituted phenyl which can be substituted by an alkyl, e.g., a methyl (CH_3). Therefore, the instantly claimed compounds differ from the reference compounds by a -CH_2 group and it is well established that compounds that differ by a –CH_2 group are structural homologs. It would have been obvious to one having ordinary skill in the art at the time of the invention to modify the reference compounds to prepare the structural homolog. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such structurally homologous compounds are expected to possess similar properties. It has been held that compounds that are structurally homologous to prior art compounds are *prima facie* obvious, absent a showing of unexpected results. *In re Hass*, 60 USPQ 544 (CCPA 1944); *In re Henze*, 85 USPQ 261 (CCPA 1950).

2. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tomiyama et al., U.S. Patent No. 4,797,415. The reference teaches benzofuran substituted phenyl compounds that are structurally analogous to instantly claimed compounds. See the structural formula (I) in col. 1 wherein Y is carbonyl and B is the substituted phenyl group wherein R^2 is –O-(CHR^3)-COR^4

wherein R^3 is H and R^4 is hydroxyamino; and the compound of Example 8. The compounds are taught to be useful as pharmaceutical therapeutic agents, see col. 1. The instant compounds differ from the reference compounds by having the $-X-CH(R^2)-CONR^3R^4$ group at a position different from the reference compounds, i.e., at the 2-position of the phenyl group as compared to the 4-position in the reference. Therefore, the instantly claimed compounds are positional isomers of the reference compounds. It would have been obvious to one having ordinary skill in the art at the time of the invention to prepare the instantly claimed compounds because they are positional isomers of the reference compounds. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such isomeric compounds are suggestive of one another and would be expected to share similar properties and therefore, the same use as taught for the reference compounds, i.e., as pharmaceutical agents. It has been held that a compound, which is structurally isomeric with a compound of prior art is prima facie obvious absent unexpected results. *In re Finley*, 81 USPQ 383 (CCPA 1949); *In re Norris*, 84 USPQ 458 (CCPA 1950); *In re Dillon*, 919 F.2d at 696, 16 USPQ2d at 1904 (Fed. Cir. 1990).

Duplicate Claims

Applicant is advised that should claims 28, 48 and 49 be found allowable, claims 29, 50 and 51 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The instant claims 29, 50 and 51 recite a mode of action or mechanism involved in the method and

the specification discloses that the mode of action is used in the method of treatment of HIV infection.

Allowable Subject Matter

Claims 2-3, 5, 9, 18-20, 23, 25, 34-36, 40, 45-47, 55, and 58-62 are allowed. Claims 7, 13, 26, 44 and 56 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The references of record do not teach or fairly suggest the claimed compounds.

Receipt is acknowledged of the Information Disclosure Statement filed on December 22, 2005 and a copy is enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deepak Rao
Primary Examiner
Art Unit 1624

March 28, 2006